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09/918,715	08/01/2001	Brad St. Croix	001107.00134	2480

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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/918,715	Applicant(s) ST. CROIX ET AL.	
	Examiner Christopher H Yaen	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *11-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 & 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I (claims 1-10) in Paper No. 12 is acknowledged. Accordingly, it is noted that applicant has elected SEQ ID No: 230 for prosecution on the merits and that is was stated that this sequence was the elected as the species. However, as stated in the action mailed 3/25/2003 (paper no. 11), the selection of the sequence was NOT to be construed as a species election, but rather a separate invention because each sequence identification number differs in structure, function, and chemical properties. As such, claims 1-10 will be examined to the extent that it reads on SEQ ID No: 230.

2. Claims 1-17 are pending, claims 11-17 are withdrawn from further consideration as being drawn to a non-elected invention. Applicant is reminded to cancel all non-elected claims.

3. Claims 1-10 with SEQ ID No: 230 are examined on the record.

Information Disclosure Statement

4. The Information Disclosure Statement filed 8/21/2001 & 7/18/2002 (paper no. 4 & 10) is acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Objections

5. Claim 1 is objected to because of the following informalities: the claim recites sequence identification numbers drawn to non-elected sequence.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The claims of the instant invention are drawn to an isolated molecule comprising an antibody variable region that binds to a TEM17 protein of SEQ ID No: 230. The disclosed utilities for antibody include using the antibody to inhibit neoangiogenesis, methods of inhibiting cancer growth through the inhibition of angiogenesis, and isolating endothelial cells that display TEM 17 on its surface. However, neither the specification nor any art of record teaches what the TEM17 protein is, what its function is within a cell, nor any well established utility. Furthermore, the specification has not taught the relationship of the protein with any specific disease nor has the specification established any specific etiology of any specific disease that is associated with the TEM17 protein. As such, antibodies developed against the protein would also have no specific or well established utility because the protein itself is not defined. Besides the fact that the characterization of the protein has not been established, there is no evidence that the protein even exists in endothelial cells associated with tumor vasculature.

The specification disclose that through SAGE analysis, the applicants were able to discover genes that were differentially expressed in normal endothelial cells verses tumor associated endothelial cells. Through this analysis, several genes were up regulated in expression when normal endothelial cells where compared with tumor

associated endothelial cells. Among these upregulated genes were TEM17, wherein the specification teaches that TEM17 expression was upregualted in several tumor types. However, because the identity of this gene is not known and because the actual protein was never isolated, there is no evidence that the protein even exists. It is well known in the art that regulation of mRNA translation is one of the major regulatory steps in the control of gene expression (Jansen, M et al, 1995, Pediatric Res, 37 (6): 681-686). Those of skill in the art recognize that expression of mRNA, in a tissue, does not dictate nor predict the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp. 2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from

patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Yokota, J et al (Oncogene, 1988,Vol.3, pp. 471-475) teach that the retinoblasma (RB) 115 kD protein is not detected in all nine cases of lung small-cell carcinoma, with either normal or abnormal size mRNA, whereas the RB protein is detected in three of four adenocarcinomas and all three squamous cell carcinomas and one of two large cell carcinomas expressing normal size RB mRNA. Thus, predictability of protein translation or the extent of translation is not solely contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Although the specification clearly demonstrates that transfected polypeptide was able to express, the claimed polypeptide was expressed using a cloning vector driven by an artificial promoter. This is not sufficient to establish that the putative polypeptide is in actuality produced *in vivo* or that it is differentially expressed in cancer cells when compared to benign lesions or that it is in any way involved in carcinogenesis or the etiology of any disease or that it is useful for any of the asserted utilities drawn to cancer. For the above reasons, one would not believe that it is more likely than not that the putative polypeptide would function as asserted.

Claims 1-10 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, 1st paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant invention is drawn to an isolated molecule comprising an antibody variable region. The specification discloses methods of SAGE analysis for the determination of varying expression levels, but nowhere in the specification does it provide one of skill in the art the evidence that the applicant was indeed in possession of an antibody that binds to TEM SEQ ID No: 230. Because the specification is devoid of such teachings, one of skill in the art cannot adequately assess whether the invention was indeed in possession of the claimed invention at the time of filing. In order for the applicant to comply with the requirements of written description, there must be evidence that at the time of filing there was possession of a molecule that comprises an antibody variable region. No such disclosure or description of a molecule is provided in the instant specification.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacobs *et al* (WO 98/14576). Claims are drawn to an isolated molecule comprising an antibody variable region which binds to the TEM protein represented by SEQ ID No: 230. Because the claims have not specifically defined the epitope region and because Jacobs *et al* discloses a protein that has an epitope that is identical to that of the instantly claimed sequence identification number, and because in the absence of evidence to the contrary, the antibody disclosed by Jacobs (see page 19) would be able to bind to the TEM protein claimed.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
August 5, 2003

ANTHONY C. [illegible]
SUPERVISORY [illegible] EXAMINER
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